REMARKS

The allegation that Kohler anticipates claims 42-43, 50-59 and 61 is unwarranted. Even if the p60 antigen used by Kohler to generate its antibodies inherently contains the peptides of SEQ ID NOs: 17, 20, 26, 29, 30 or 31, the resultant antiserum does not anticipate the current claims. The latter are drawn to an antibody having the recited specificity, *i.e.*, to only one peptide among those listed. Kohler's antisera contain a mixture of antibodies having multiple specificities. Support for the amendment is clear, *e.g.*, from the examples which all utilize only one peptide.

Moreover, in order to be anticipatory, the claimed invention must necessarily and inevitably flow from what is described in the reference. The Examiner has not met her burden to prove inherent anticipation in this case because nothing in the prior art leads a skilled worker inexorably to any of the claimed antibodies.

As for the obviousness rejection, this, too, is untenable. The cited references do not render obvious claims 60 and 62 (which are drawn to monoclonal antibodies) as alleged by the Examiner. Nor do the references of record, taken individually or in combination, render obvious any of the other claims.

The Examiner alleges that it would be obvious from Kohler and Lerner to generate antibodies against intact p60 and then to determine which p60 epitopes bind to those antibodies. However, Kohler provides no motivation to select from the polyspecific mixture of antibody molecules present in such a polyclonal antibody an antibody molecule which is reactive to the particular epitopes recited in the instant claims.

Not only would it not be obvious from the cited references to use the method suggested by the Examiner, but Kohler and Lerner fail to teach *any* method that would generate the claimed isolated antibodies. The cited references do not suggest or disclose using the specific p60 peptides which are taught by, and claimed in, the instant invention to generate isolated antibodies; and they do not provide a reasonable expectation that those peptides would be successful in generating antibodies. Therefore, the references do not suggest or disclose the invention.

A skilled worker would not know from Kohler and Lerner which of the many possible p60 peptides to use as immunogens. In fact, the specification teaches that only a small subset of peptides can be used successfully to generate the antibodies of the invention. See, *e.g.*,

page 11, lines 5-10. In support of this statement from the specification is the attached Declaration by Dr. Bubert, an inventor and an expert in the field, which shows that only a small subset of the numerous L. monocytogenes-specific p60 peptides are suitable for the preparation of the claimed antibodies. See, *e.g.*, Appendix 1 to the Declaration, which shows that of eight out the many possible peptides which were tested, only two exhibited the desired antigenicity.

Furthermore, a variety of references in the scientific literature report that it is extremely difficult to predict whether a particular peptide will have a structure that is suitable for generating an antibody, based solely on the sequence of a protein of interest. Some such studies (*e.g.*, papers by Nestorowicz *et al.* and van Regenmortel *et al.*) are reviewed by Dr. Neumann in a Declaration which was originally submitted in an ancestor of the present application, Ser. No. 08/075,248. A copy of that Declaration, and copies of Nestorowicz *et al.* and van Regenmortel *et al.*, are attached for the convenience of the Examiner. Dr. Neumann concludes, *i.a.*, that Lerner's assumption that practically all peptides derived from the sequence of a given protein can give rise to antibodies which react with that protein is incorrect.

The combination of Kohler and Lerner provides at most a suggestion to try immunizing with the plethora of peptides found within the L. monocytogenes-specific p60 sequences. It clearly does not provide motivation to use the specific peptides which the inventors have shown to be useful for generating the antibodies of the invention, and it does not provide the requisite reasonable expectation of success. Therefore, these references do not render the instant claims obvious. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

Not only is there not a case of *prima facie* obviousness, but even if there were, the invention provides advantages, as noted in the specification, *e.g.*, at page 3, first paragraph. For example, the instant invention allows one to prepare a polyclonal antibody having specificities only against a particular peptide of interest, whereas methods in which antibodies are generated against full length p60 require complex purification procedures in order to isolate antibody molecules having the desired specificity, and they require making large amounts of the polyclonal antibody to be purified.

The secondary references drawn to methods of generating monoclonal antibodies do not remedy the deficiencies of Kohler and Lerner as discussed above. Therefore, the

secondary references do not, in combination with those references, render claims 60 and 62 obvious.

The rejections should be withdrawn.

Respectfully submitted,

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MARKED-UP VERSION

42. (Twice Amended) An isolated antibody which specifically binds to the p60 protein from pathogenic listeria, wherein said antibody binds an epitope from ~~the~~ only one of the following peptides: ; SEQ ID NO: 17, 20, 26, 29, 30 or 31.

43. (Amended) An isolated antibody which can be prepared by immunizing an experimental animal with only one of the following peptides: ; SEQ ID NO: 17, 20, 26, 29, 30 or 31, or with an immunogenic conjugate which comprises only one of the following peptides: ; SEQ ID NO: 17, 20, 26, 29, 30 or 31, wherein said antibody specifically binds to the p60 protein from pathogenic listeria.

Since claims 63- 70 are newly added, no marked-up version of these claims is necessary.